AF

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,162	10/31/2002	Mario A Bourdon	LJIEM110-1	8841

7590 11/25/2005

Pillsbury Winthrop
50 Fremont Street
San Francisco, CA 94120

EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 11/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/701,162	BOURDON ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2005*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-29* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The special technical feature that appears to link claims 1-29 is a method for inhibiting a host cell angiogenic effect. References Borgstrom et al. (March-April 1993), Ferrera (1995) and DiPietro et al. (1993) disclose methods for inhibiting angiogenesis comprising inhibiting a host cell angiogenic effect that is the same as claimed. Borgstrom teaches administering an agent (Linomide) to a cellular system that inhibits angiogenesis. Ferrara teaches administering an agent (anti-VEGF) to endothelial cells to inhibit angiogenesis. DiPietro teaches administering an agent (thrombospondin-1) to activated macrophages to inhibit angiogenesis. Therefore the technical feature recited in claims 1-29 is not a contribution over the prior art. Accordingly, the groups set forth below are not so linked as to form a single inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 2-12, drawn to a method for inhibiting angiogenesis by inhibiting a mast cell.

Group II, claim(s) 2-12, drawn to a method for inhibiting angiogenesis by inhibiting a macrophage.

Group III, claim(s) 2-12, drawn to a method for inhibiting angiogenesis by inhibiting a fibroblast.

Group IV, claim(s) 2-12, drawn to a method for inhibiting angiogenesis by inhibiting an endothelial cell.

Group V, claims(s) 13-20, drawn to a method for inhibiting angiogenesis by depletion of activated macrophages.

Group VI, claims 13, 14, 21 and 22, drawn to a method for inhibiting angiogenesis by inhibiting macrophage activation.

Group VII, claims 13, 14, 23-25, drawn to a method for inhibiting angiogenesis by inhibiting monocyte recruitment.

Group VIII, claim 26, drawn to a method for inhibiting angiogenesis in a tumor.

Group IX, claim 26, drawn to a method for inhibiting angiogenesis in wound-surrounding cells.

Group X, claim 26 in part, drawn to a method for inhibiting angiogenesis for cells characteristic of a proliferative disorder.

Group XI, claims 27-29, drawn to a method for inhibiting angiogenesis by inhibiting M-CSF gene expression.

Claim 1 (process for inhibiting host cell angiogenic effect) links inventions for processes of inhibiting angiogenesis of Groups I-XI. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claims, Claim 1. Upon the allowance of the linking claims, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise including all

the limitations of the allowable linking claims will be entitled to examination in the instant application. Applicants are advised that if any such claims depending from or including all the limitations of the allowable linking claims is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or non-statutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-132 (CCPA 1971). See also MPEP § 804.01.

The methods of Inventions I-XI differ in the method objectives, method steps and parameters and in the reagents used. Invention I recites inhibiting a mast cell angiogenic effect; Invention II recites inhibiting a macrophage angiogenic effect; Invention III recites inhibiting a fibroblast angiogenic effect; Invention IV recites inhibiting a endothelial cell angiogenic effect; Invention V recites inhibiting angiogenesis by macrophage depletion; Invention VI recites inhibiting angiogenesis by inhibiting macrophage activation; Invention VII recites inhibiting angiogenesis by inhibiting macrophage recruitment; Invention VIII recites inhibiting tumor angiogenesis; Invention IX recites inhibiting wound-surrounding cell angiogenesis; Invention X recites inhibiting proliferative cell disorder angiogenesis; and Invention XI recites inhibiting M-CSF gene expression to inhibit angiogenesis. The examination of all groups would require different searches in the U.S. PATENT shoes and the scientific literature and would require the consideration of different patentability issues. Thus Inventions I-XI are separate and distinct in having method steps and different endpoints and are patentably distinct.

If any one of Groups I-IV is elected then species (angiogenic factor) below must be elected as applicable. This application contains claims directed to the following patentably distinct species of the claimed invention:

Specie A) VEGF

Specie B) bFGF

Specie C) IL-8

Specie D) angiostatin.

Species A-D are separate and distinct cytokine and/or growth factors, each having their own receptors and possessing different structural and functional characteristics. For example, refer to the Human Protein Reference Database, which lists their respective tissue distribution patterns, molecular class, molecular function, biological process and disease correlates. As a result, due to the different and distinct properties required for each species, searching all of the species would be an undue search burden upon the examiner.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claim 1 is generic to species A-D.

If Group V is elected then species (activated macrophage depleting agent) below must be elected as applicable. This application contains claims directed to the following patentably distinct species of the claimed invention:

Species A1) etidronate disodium

Species B1) (3-amino-1hydroxy-propylidene)-1, 1-diphosphanate.

Etidronate, a first-generation, non-N-containing diphosphonate (R_2= CH_3) compound is incorporated by the cell into ATP and upon accumulation in cells results in death. Pamidronate ((3-amino-1hydroxy-propylidene)-1, 1-diphosphanate) is a second-generation N-containing diphosphonate (R_2=$CH_2CH_2NH_2$) compound that inhibits enzymes in the biosynthetic pathway for production of cholesterol and isoprenoid compounds, which are required for post-translational modification of small GTPases. Small GTPases are signaling proteins that regulate a number of cell processes such as membrane ruffling, cytoskeletal organization and vesicle trafficking. Thus, the species A1 and B1 are chemically, structurally and functionally different from each other. As a result, due to the different and distinct properties required for each species, searching all of the species would be an undue search burden upon the examiner.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claim 13 is generic to species A1 and B1.

If Group VI is elected then species (monocyte activation preventing agents) below must be elected as applicable. This application contains claims directed to the following patentably distinct species of the claimed invention:

A2) small molecule mimetics

B2) M-CSF blocking agents

C2) anti-M-CSF receptor antibodies

D2) M-CSF antagonists

E2) M-CSF receptor antagonists

The small molecule mimetic, the blocking agent, the receptor antibody, the antagonist and the receptor antagonist of species A2-E2, respectively, are all chemically and structurally different from each other. Additionally, the small molecule mimetic is any low molecular-weight drug that acts at M-CSF receptors as agonists, inverse agonists or antagonists that inhibit or modify M-CSF-related signal transduction in monocyte activation. M-CSF blocking agents can include antibodies, synthetic or recombinant peptides or small molecule drugs that may act at M-CSF receptors and/or possibly even other receptors, as agonists, inverse agonists or antagonists that inhibit or modify M-CSF-related signal transduction in monocyte activation. The anti-M-CSF receptor antibody is specific for targeting the M-CSF receptor in its ability to inhibit or modify M-CSF-related signal transduction in monocyte activation. The M-CSF antagonist can include antibodies, synthetic or recombinant peptides or small molecule drugs that inhibit or modify M-CSF-related signal transduction in monocyte activation at M-CSF receptors and/or possibly even other receptors. Finally, M-CSF receptor antagonists can include antibodies, synthetic or recombinant peptides or small molecule drugs that act at M-CSF receptors to inhibit or modify M-CSF-related signal transduction in monocyte activation. As a result, due to the different and distinct properties required for each species, searching all of the species would be an undue search burden upon the examiner.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claim 13 is generic to species A2-E2.

If Group VII is elected, then species (monocyte recruiting preventing agents) below must be elected as applicable. This application contains claims directed to the following patentably distinct species of the claimed invention:

Specie A3) antibodies

Specie B3) small molecule mimetics

Specie C3) monocyte rolling preventing agents

The species of A3-C3 are all chemically and structurally different from each other. Additionally, the antibodies that prevent monocyte recruitment can be specific for any number of cytokines, growth factors or surface signaling molecules on monocytes (or even other interacting cells in a microenvironment) that are involved in pathways initiating monocyte recruitment. Small molecule mimetics are any low molecular-weight drugs that act as agonists, inverse agonists or antagonists that inhibit or modify signal transduction in monocyte recruitment. Finally, monocyte rolling preventing agents would be those agents having the ability to both prevent monocyte rolling and monocyte recruitment. As a result, due to the different and distinct properties required for each species, searching all of the species would be an undue search burden upon the examiner.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claim 13 is generic to species A3-C3.

If Group VII is elected then species (monocyte rolling preventing agents) below must be elected as applicable. This application contains claims directed to the following patentably distinct species of the claimed invention:

Specie A4) anti-P selectin antibody

Specie B4) anti-E selectin antibody

Specie C4) selectin antagonists

In mice deficient for P-selectin, it is necessary to block E-selectin function to significantly reduce rolling, and in E-selectin knockouts, an antibody against P-selectin must be introduced to reduce rolling. Although P- and E-selectin seem to have redundant functions, observations of rolling flux fraction and rolling velocity indicate that P-selectin is responsible for early rolling while E-selectin allows slow rolling and more adhesion. Thus, species to an antibody for P selectin and an antibody for E-selectin would be distinct in their chemical structure, target molecule recognition and mechanism of action. Selectin antagonists are compounds (e.g., antibodies, recombinant proteins and small molecule drugs) that mimic the adhesion molecules (or portions thereof) that bind to selectins and prevent rolling or tethering of leukocytes. Thus, the species A4-C4 are chemically, structurally and functionally different from each other. As a result, due to the different and distinct properties required for each species, searching all of the species would be an undue search burden upon the examiner.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claim 13 is generic to species A4-C4.

If Group IX is elected then species (M-CSF gene expression preventing agent) below must be elected as applicable. This application contains claims directed to the following patentably distinct species of the claimed invention:

Specie A5) retrovirus

Specie B5) adenovirus

The retrovirus specie is any group of enveloped, double-stranded RNA viruses containing reverse transcriptase, and which may cause tumors. The adenovirus specie is any group of non-enveloped icosahedral DNA virus containing DNA, and which may produce respiratory tract diseases. Thus, the species A5 and A6 are chemically, structurally and functionally different from each other. As a result, due to the different and distinct properties required for each species, searching all of the species would be an undue search burden upon the examiner.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claim 27 is generic to species A5 and B5.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include

all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

CONCLUSION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached between 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

LAB

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER